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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	

ART UNIT	PAPER NUMBER
1795	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,076	RUBIN ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/23/2010 (RCE and amndt.)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment received on June 23, 2010 does not render the application allowable. Contrary to Applicant's assertions the prior art, as discussed in the rejections below, also disclose or render obvious the new limitation to claim 1 added by the latest amendment.

Specification

2. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously

incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f). Applicant has amended claim 1 to require

> wherein the one or more pH active groups is linked to the substrate via at least one group chosen from one or more linker molecules, one or more layers of the separating coating, or a combination thereof, and via at least one quinone, ...

Support for this amendment stated to be page 5, lines 24-31, of the specification, and Examples 1 and 2. However, page 5, lines 24-31, of the specification only refers to Danish patent application DK PA2002 00875 for instructions on how to make the claimed links. Examples 1 and 2 only mention using quinone. Moreover, the quinone does not appear to be for linking any pH active groups as the quinone is used to functionalise material H1010, which is located in circular separating groove 1, while the pH active groups (IEF electrode strip and gel) are located in grooves 6 and 7, that is, separate from quinine functionalized material H1010.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. Applicant has amended claim 1 to require

> wherein the one or more pH active groups is linked to the substrate via at least one group chosen from one or more linker molecules, one or more layers of the separating coating, or a combination thereof, and via at least one quinone, ...

Support for this amendment stated to be page 5, lines 24-31, of the specification, and Examples 1 and 2. However, page 5, lines 24-31, of the specification only refers to Danish patent application DK PA2002 00875 for instructions on how to make the claimed links. Examples 1 and 2 only mention using quinone. Moreover, the quinone does not appear to be for linking any pH active groups as the quinone is used to functionalise material H1010, which is located in circular separating groove 1, while the pH active groups (IEF electrode strip and gel) are located in grooves 6 and 7, that is, separate from quinine functionalized material H1010. Thus, Applicant's only guidance on how to make a link of the one or more pH active groups to the substrate via one of the listed groups is reference to Danish patent application DK PA2002 00875. Since Applicant views feature added by amendment as being inventive over the prior art and non-obvious Applicant's silence on how to link the one or more pH active groups via one the listed groups renders the claim not enabled.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wiktorowicz et al. US 6,214,191 B1 ("Wiktorowicz") in view of Zanzucchi et al. US 5,755,942 ("Zannzucchi") and Simpson et al. US 6,143,152 ("Simpson"), and Cahill et al. EP 1044716 A1 ("Cahill").

Wiktorowicz discloses a micro fluid biomolecule separation system (abstract) comprising a primary separating path (160) and one or more secondary process paths (170), said primary separating path being in the form of a separating coating carried on a substrate (col. 06:61-67 and col. 10:01-08), wherein said separating coating comprising one or more separating layers (col. 10:01-08), at least one separating layer consisting of or comprises one or more pH active components comprising pH active groups defined as chemical groups that are capable of being protonated or deprotonated in aqueous environments (col. 06:61-67 and col. 10:01-08), and wherein the one or more pH active groups is linked to the substrate via at least one or more linker molecules ("According to a preferred embodiment, the second electrophoresis region includes an isoelectric focusing region that contains a continuous pKa gradient immobilized on at least one of the major surfaces ... [emphasis added]" "The buffering compounds may be coupled directly to the IEF regions of the plates using suitably activated plates or buffering compounds, or may be attached via a cross-linking reagent ... [emphasis added]" "The assembly is allowed to incubate at a suitable temperature until the pKa buffering compounds become bound to the surface-activated allyl groups. [emphasis added]" "Attachment of the immobilines was accomplished as follows. First

allyl methacrylate moieties were attached to the entire separation cavity ...[emphasis added]" See Wiktorowicz col. 08:61-66; col. 09:53-65; col. 10:60-63; col. 10:14-65; and col. 17:20-23.) said fluid biomolecule separation system comprises means for applying a voltage over the primary separating path (col. 07:35-52), the or each secondary process path(s) comprising one or more inlets in liquid communication with the primary separating path, said one or more inlets being placed along or extends along the primary separating path (note inlets for microchannels 170 along upper edge 126a), whereby biomolecules separated along the primary path is capable of being introduced into the secondary process path(s) for being processed further (col. 07:47-54).

. Wiktorowicz does not mention (1) the thickness of the separating coating, and (2) having the system be in the form of a disc device begin essentially circular comprising a centre, the microchannel structure being arranged around the centre.

As for the claimed coating thickness range it should be first noted that the separating coating in Wiktorowicz may be an isoelectric focusing pKa gradient. See col. 06:61-67; col. 06:06-14; and col. 09:58 – col. 10:25. Cahill discloses isoelectric focusing pKa gradient coatings for use in electrophoresis microchannels. See the abstract. The coatings disclosed by Cahill may be used in microchannels having a height of only 10 nm. See paragraphs [0010] and [0020]. Since Cahill states, "The distance between the surfaces is typically between 10 and 1000 nm [0.01 – 1.00 μm], especially between 10 and 500 nm [0.01 – 0.50 μm]" and "One or both surfaces may comprise a coating of buffering molecules" (paragraph [0010]), Cahill thus implicitly

discloses separating coatings with a thickness between 0.01 and 15 μm. Therefore, Cahill implicitly discloses separating coatings with a thickness between 0.01 and 15 μm. Thus, in light of Cahill to use isoelectric focusing coatings having a thickness between 0.01 and 15 μm is merely simple substitution of one known element for another to obtain predictable results. Moreover, an advantage of the separating coatings Cahill discloses is that they avoid material losses that occur in other types of pH gradients due to solid pH barriers formed in gels and membranes. See [0006]. Additionally, Cahill discloses having the one or more pH active groups linked to the substrate via at least linker molecules: 'Said pH buffers are formed by buffer molecules, which are fixed on surfaces bordering the electrophoretic volume. By the word "fixed" is meant, that the buffer molecules are bound or ligated to said surfaces ... [emphasis added]" See paragraph [0009]. "The buffer molecules need not be immobilines, ... Instead they consist especially of a skeleton or backbone chain of hydrocarbon- or fluorocarbon-based molecules with terminal buffer groups which have been attached, especially by covalently bonding, to the surface of preferentially a chip by e.g. photoetching, derivatisation methods, micro-contact printing, self assembly monolayer reactions, or other prior art methods. By self assembly monolayer is meant a system where a surface is functionalized to allow covalent bonding to one or more types of specific substrate molecules, such that the surface binds substrate in a specific manner, ..." See paragraph [0011]. Also, "In a preferred variant of the invention the array is created using suitable precursors and microcontact printing, self-assembly reactions, or photo-

activated chip technology where reactions take place in photo-activated regions, ..." See paragraph [0031].

As for having the system be in the form of a disc device begin essentially circular comprising a centre, the microchannel structure being arranged around the centre, Wiktorowicz has the system in the form of a disc device begin essentially rectangular comprising a centre, the microchannel structure being arranged around the centre. See Figures 3 and 4. Changing the shape of the disc form rectangular to circular is a mere matter of choice that has no effect on the operation of the device. MPEP 2144.04.IV.B. Moreover as shown by Simpson and Zanzucchi it was known at the time of the invention to have a microfluidic system be in the form of a disc device begin essentially circular comprising a centre, the microchannel structure being arranged around the centre. See Figure 1 in Simpson and Figure 1B in Zanzucchi. Thus, the substitution of a circular disc for a rectangular disc is also simple substitution of one known element for another to obtain predictable results.

9. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al.

US 6,676,819 B1 ("Liu"), Zanzucchi et al. US 5,755,942 ("Zannzucchi"), Simpson et al. US 6,143,152 ("Simpson"), Cahill et al. EP 1044716 A1 ("Cahill"), and newly cited Rosengren et al. US 4,130,470 ("Rosengren").

Liu discloses a micro fluid biomolecule separation system (abstract and col. 01:34-44) comprising a primary separating path (14) and one or more secondary process paths (60), said primary separating path being in the form of a separating coating carried on a substrate (col. 10:60 – col. 11:26), wherein said separating coating comprising one or more separating layers (col. 10:60 – col. 11:26), at least one separating layer consisting of or comprises one or more pH active components comprising pH active groups defined as chemical groups that are capable of being protonated or deprotonated in aqueous environments (col. 10:60 – col. 11:26 and col. 02:30-60), wherein the one of more pH active groups is linked to eh substrate via at least one group chosen from one or more linker molecules or one or more layers of the separating coating ("It is current practice to create IPG gels in a thin planar configuration bonded to an inert plastic sheet that has been treated for chemical binding to an acrylamide gel." See Liu col. 02:45-47. Liu also refers to Rosengren for immobilizing the pH active groups. See Liu col. 02:30-40. Rosengren states, "The immobilization [of the pH active groups] is achieved by means of affixing the groups to or into a matrix which could also constitute the convection stabilizing medium in the separation. This matrix could preferably be formed by a material which in combination with the separation medium gives rise to a gel." See col. 02:38-43.) said fluid biomolecule separation system comprises means for applying a voltage over the primary separating

path (col. 10:18-30 and col. 13:01-09), the or each secondary process path(s) comprising one or more inlets in liquid communication with the primary separating path, said one or more inlets being placed along or extends along the primary separating path (note inlets for microchannels 60 especially in Figures 5, 6, 8, 9A, 9B, and 10-12), whereby biomolecules separated along the primary path is capable of being introduced into the secondary process path(s) for being processed further (col. 13:15-30 and col. 14:05-15).

As for the claimed coating thickness range it should be first noted that the separating coating in Liu may be an isoelectric focusing pKa gradient. See Col. 11:11-26. Cahill discloses isoelectric focusing pKa gradient coatings for use in electrophoresis microchannels. See the abstract. The coatings disclosed by Cahill may be used in microchannels having a height of only 10 nm. See paragraphs [0010] and [0020]. Since Cahill states, "The distance between the surfaces is typically between 10 and 1000 nm [0.01 – 1.00 μm], especially between 10 and 500 nm [0.01 – 0.50 μm]" and "One or both surfaces may comprise a coating of buffering molecules" (paragraph [0010]), Cahill thus implicitly discloses separating coatings with a thickness between 0.01 and 15 μm. Therefore, in light of Cahill to use isoelectric focusing coatings having a thickness between 0.01 and 15 μm is merely simple substitution of one known element for another to obtain predictable results. Moreover, an advantage of the separating coatings Cahill discloses is that they avoid material losses that occur in other types of pH gradients due to solid pH barriers formed in gels and membranes. See [0006]. Additionally, Cahill discloses having the one or more pH active groups linked to

the substrate via at least linker molecules: 'Said pH buffers are formed by buffer molecules, which are fixed on surfaces bordering the electrophoretic volume. By the word "fixed" is meant, that the buffer molecules are bound or ligated to said surfaces ... [emphasis added]" See paragraph [0009]. "The buffer molecules need not be immobilines, ... Instead they consist especially of a skeleton or backbone chain of hydrocarbon- or fluorocarbon-based molecules with terminal buffer groups which have been attached, especially by covalently bonding, to the surface of preferentially a chip by e.g. photoetching, derivatisation methods, micro-contact printing, self assembly monolayer reactions, or other prior art methods. By self assembly monolayer is meant a system where a surface is functionalized to allow covalent bonding to one or more types of specific substrate molecules, such that the surface binds substrate in a specific manner, ..." See paragraph [0011]. Also, "In a preferred variant of the invention the array is created using suitable precursors and microcontact printing, self-assembly reactions, or photo-activated chip technology where reactions take place in photo-activated regions, ..." See paragraph [0031].

As for having the system be in the form of a disc device begin essentially circular comprising a centre, the microchannel structure being arranged around the centre, Liu has the system in the form of a disc device begin essentially rectangular comprising a centre, the microchannel structure being arranged around the centre. See Figures 3 and 4. Changing the shape of the disc form rectangular to circular is a mere matter of choice that has no effect on the operation of the device. MPEP 2144.04.IV.B. Moreover as shown by Simpson and Zanzucchi it was known at the time of the

invention to have a microfluidic system be in the form of a disc device begin essentially circular comprising a centre, the microchannel structure being arranged around the centre. See Figure 1 in Simpson and Figure 1B in Zanzucchi. Thus, the substitution of a circular disc for a rectangular disc is also simple substitution of one known element for another to obtain predictable results.

10. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. US 6,974,526 B2 ("Lee"), Zanzucchi et al. US 5,755,942 ("Zannzucchi"), Simpson et al. US 6,143,152 ("Simpson"), and Cahill et al. EP 1044716 A1 ("Cahill").

Lee discloses a micro fluid biomolecule separation system (abstract) comprising a primary separating path (3) and one or more secondary process paths (4), said primary separating path being in the form of a separating coating carried on a substrate (col. 05:45-50 and claims 2 and 9), wherein said separating coating comprising one or more separating layers (col. 10:60 – col. 11:26), at least one separating layer consisting of or comprises one or more pH active components comprising pH active groups defined as chemical groups that are capable of being protonated or deprotonated in aqueous environments (col. 10:60 – col. 11:26), said fluid biomolecule separation system comprises means for applying a voltage over the primary separating path (col. 04:21-24), the or each secondary process path(s) comprising one or more inlets in liquid communication with the primary separating path, said one or more inlets being

placed along or extends along the primary separating path (see Figures 2-9), whereby biomolecules separated along the primary path is capable of being introduced into the secondary process path(s) for being processed further (col. 02:01-19 and claim 7). As for the claimed coating thickness range it should be first noted that the separating coating in Liu may be an isoelectric focusing pKa gradient. See col. 05:45-50 and claims 2 and 9. Cahill discloses isoelectric focusing pKa gradient coatings for use in electrophoresis microchannels. See the abstract. The coatings disclosed by Cahill may be used in microchannels having a height of only 10 nm. See paragraphs [0010] and [0020]. Since Cahill states, "The distance between the surfaces is typically between 10 and 1000 nm [0.01 – 1.00 μm], especially between 10 and 500 nm [0.01 – 0.50 μm]" and "One or both surfaces may comprise a coating of buffering molecules" (paragraph [0010]), Cahill thus implicitly discloses separating coatings with a thickness between 0.01 and 15 μm. Therefor, Cahill implicitly discloses separating coatings with a thickness between 0.01 and 15 μm. Thus, in light of Cahill to use isoelectric focusing coatings having a thickness between 0.01 and 15 μm is merely simple substitution of one known element for another to obtain predictable results. Moreover, an advantage of the separating coatings Cahill discloses is that they avoid material losses that occur in other types of pH gradients due to solid pH barriers formed in gels and membranes. See [0006]. Additionally, Cahill discloses having the one or more pH active groups linked to the substrate via at least linker molecules: 'Said pH buffers are formed by buffer molecules, which are fixed on surfaces bordering the electrophoretic volume. By the word "fixed" is meant, that the buffer molecules are bound or ligated to said surfaces

... [emphasis added]" See paragraph [0009]. "The buffer molecules need not be immobilines, ... Instead they consist especially of a skeleton or backbone chain of hydrocarbon- or fluorocarbon-based molecules with terminal buffer groups which have been attached, especially by covalently bonding, to the surface of preferentially a chip by e.g. photoetching, derivatisation methods, micro-contact printing, self assembly monolayer reactions, or other prior art methods. By self assembly monolayer is meant a system where a surface is functionalized to allow covalent bonding to one or more types of specific substrate molecules, such that the surface binds substrate in a specific manner, ..." See paragraph [0011]. Also, "In a preferred variant of the invention the array is created using suitable precursors and microcontact printing, self-assembly reactions, or photo-activated chip technology where reactions take place in photo-activated regions, ..." See paragraph [0031].

As for having the system be in the form of a disc device begin essentially circular comprising a centre, the microchannel structure being arranged around the centre, Lee has the system in the form of a disc device begin essentially rectangular comprising a centre, the microchannel structure being arranged around the centre. See Figures 3 and 4. Changing the shape of the disc form rectangular to circular is a mere matter of choice that has no effect on the operation of the device. MPEP 2144.04.IV.B. Moreover as shown by Simpson and Zanzucchi it was known at the time of the invention to have a microfluidic system be in the form of a disc device begin essentially circular comprising a centre, the microchannel structure being arranged around the centre. See Figure 1 in Simpson and Figure 1B in Zanzucchi. Thus, the substitution of

a circular disc for a rectangular disc is also simple substitution of one known element for another to obtain predictable results.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Alex Noguerola/
Primary Examiner, Art Unit 1795
July 17, 2010